Using NCBI's MedGen in Clinical Practice

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Using NCBI's MedGen in Clinical Practice

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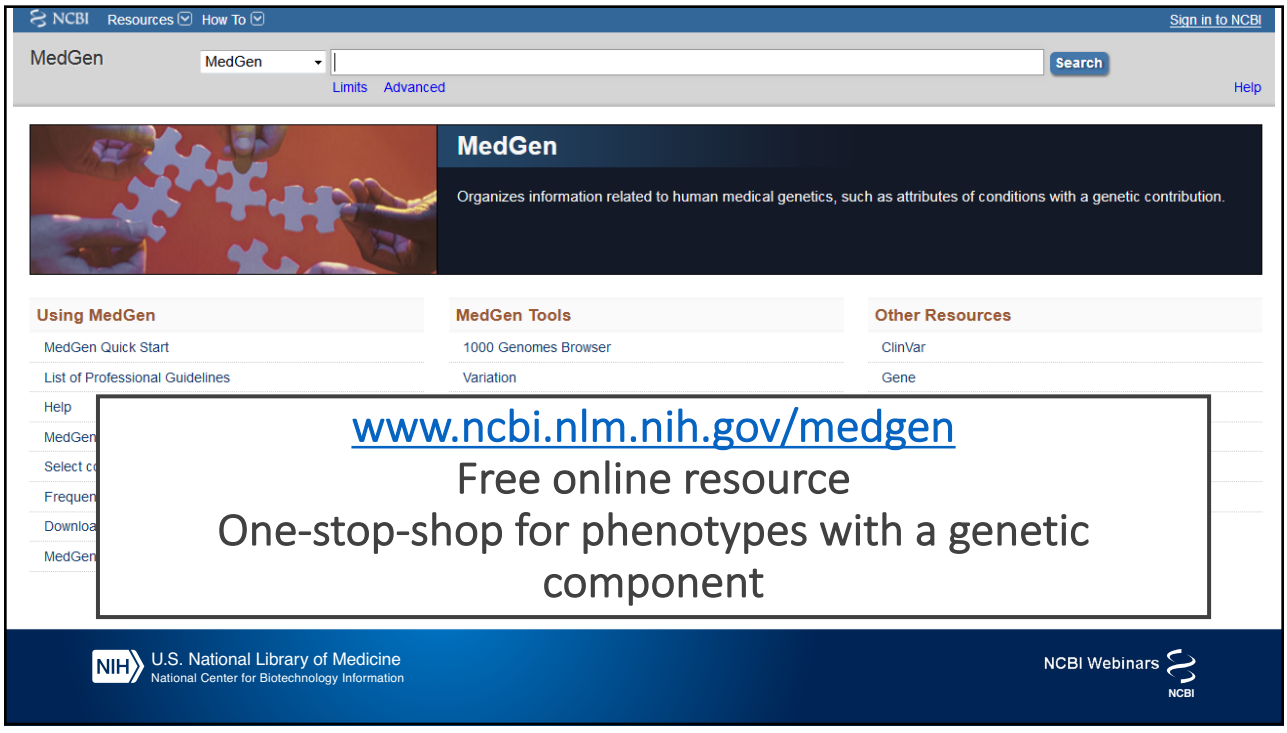
Goals

- Overview of MedGen
  - Understand its content
- Learn how to search and navigate MedGen
- Identify ways to incorporate MedGen in the clinical genetics process



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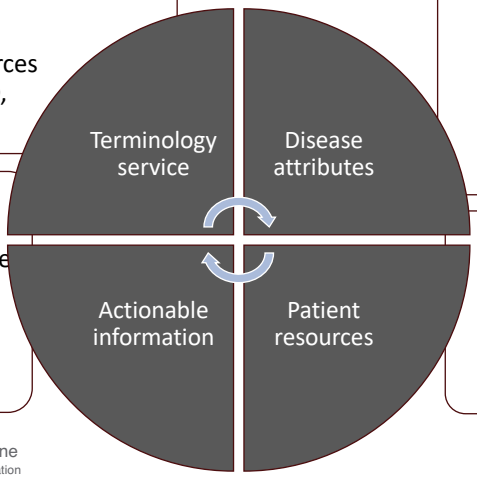
Types of records

- Mendelian disorders
- Pharmacogenetic responses
- Complex diseases with a genetic component
- Clinical features

What content is on a MedGen record?

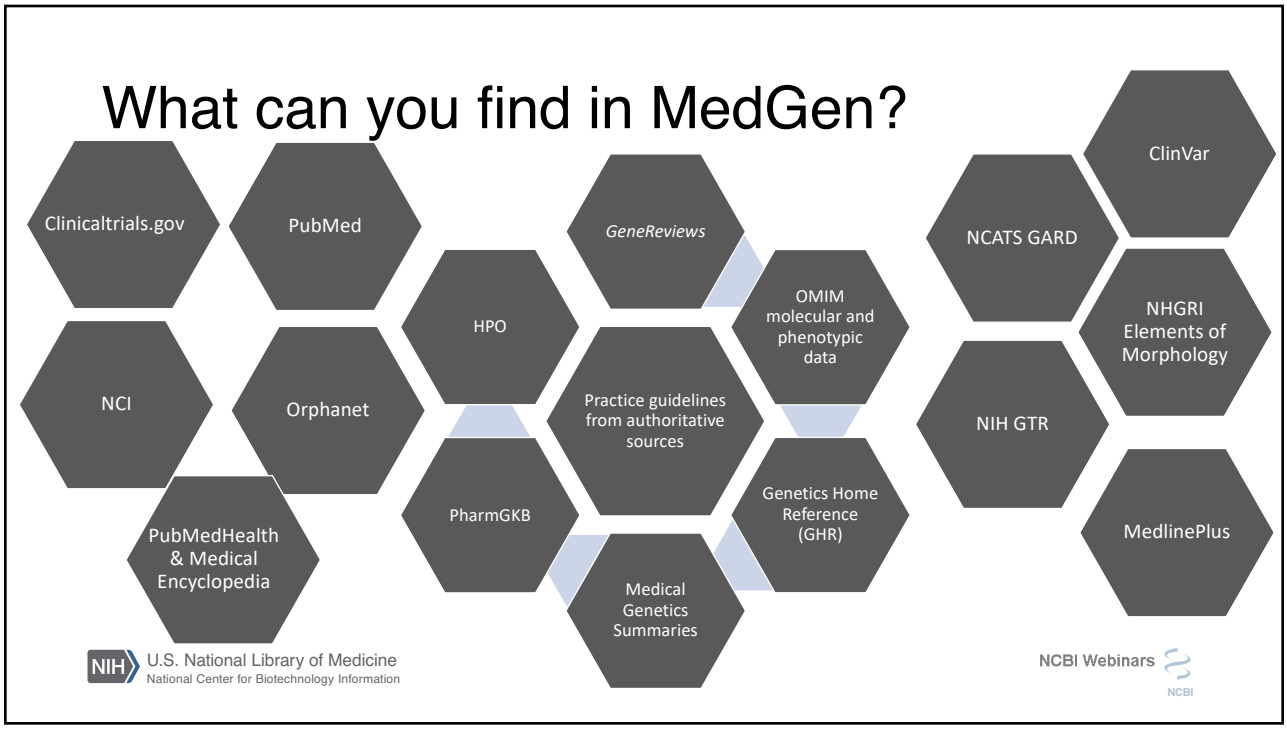
- Name
- Synonyms
- Identifiers from different sources (eg. SNOMED CT, OMIM, HPO, Orphanet, UMLS)



- Gene(s)
- Mode of inheritance
- Descriptions (e.g. OMIM, *GeneReviews*, Medical Genetics Summaries)
- Clinical features
- Disease hierarchy

- Practice guidelines
- Therapeutic recommendations for pharmacogenetic phenotype
- Clinicaltrials.gov
- Links to available tests in GTR
- Links to variants in causative gene(s) in ClinVar

- Genetics Home Reference (GHR)
- MalaCards
- MedlinePlus
- Office of Rare Diseases Research (GARD)
- Genetic Alliance


What can you find in MedGen?
Clinicaltrials.gov
PubMed
NCI
Orphanet
PubMedHealth & Medical Encyclopedia
HPO
PharmGKB
GeneReviews
OMIM molecular and phenotypic data
Practice guidelines from authoritative sources
Genetics Home Reference (GHR)
Medical Genetics Summaries
ClinVar
NCATS GARD
NHGRI Elements of Morphology
NIH GTR
MedlinePlus
NIH U.S. National Library of Medicine
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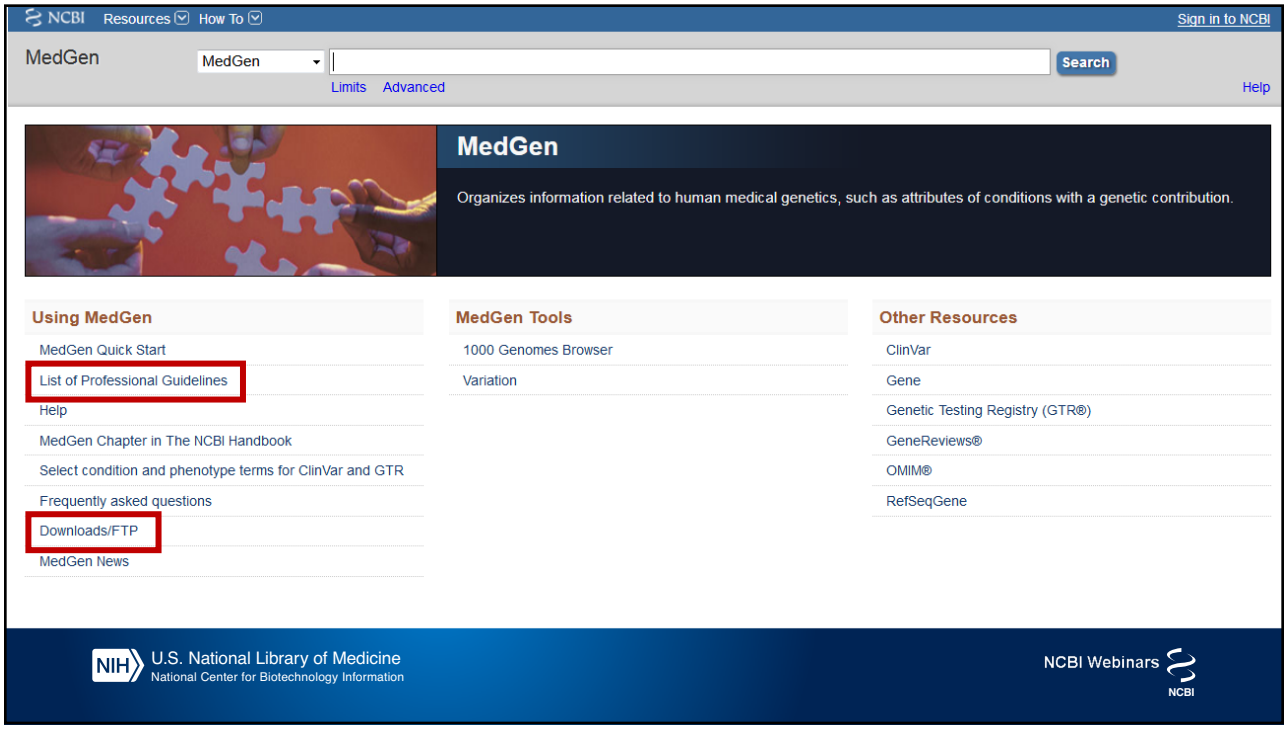
NCBI Resources How To
Sign in to NCBI
MedGen
MedGen
Search
Limits Advanced
Help
MedGen
Organizes information related to human medical genetics, such as attributes of conditions with a genetic contribution.
Using MedGen
MedGen Quick Start
List of Professional Guidelines
Help
MedGen Chapter in The NCBI Handbook
Select condition and phenotype terms for ClinVar and GTR
Frequently asked questions
Downloads/FTP
MedGen News
MedGen Tools
1000 Genomes Browser
Variation
Other Resources
ClinVar
Gene
Genetic Testing Registry (GTR®)
GeneReviews®
OMIM®
RefSeqGene
NIH U.S. National Library of Medicine
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Simple search

- Condition name & acronym
- Drug response
- Clinical feature
- Gene
- OMIM #

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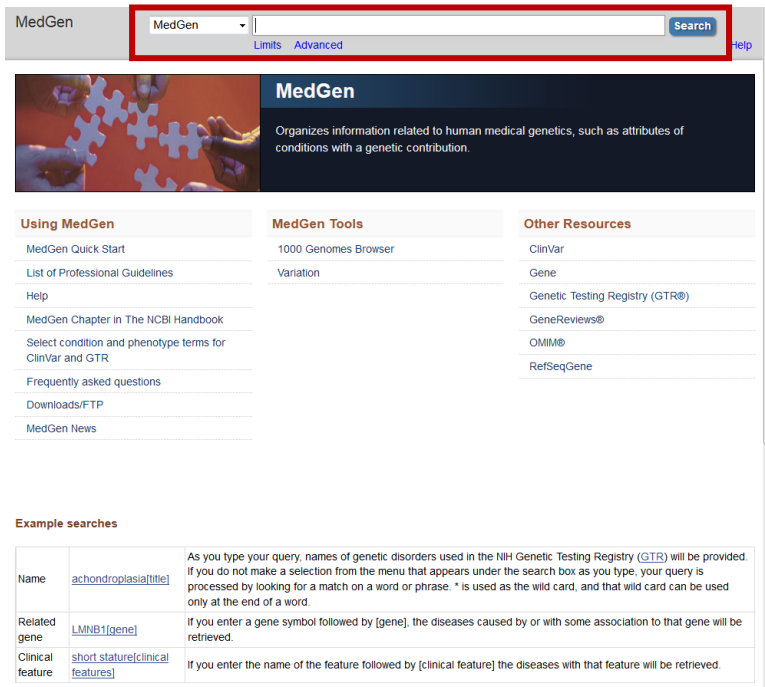

Search by clinical features

Get a list of conditions with the clinical feature derived from data from HPO and OMIM

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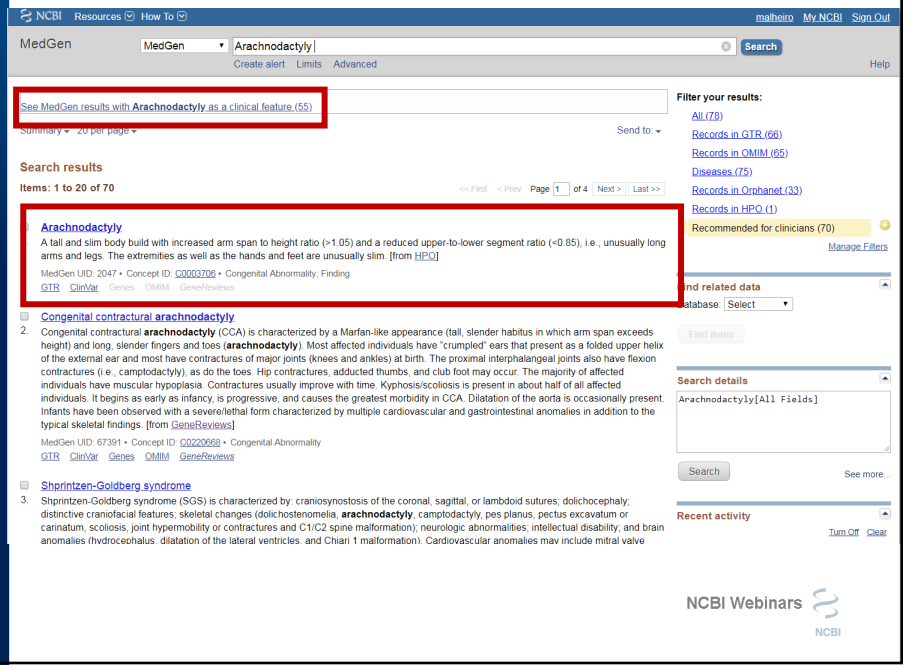

Clinical feature record

Arachnodactyly

MedGen UID: 2047 • Concept ID: C0003706 • Congenital Abnormality; Finding

Synonyms: Long slender fingers; Spider slender fingers

SNOMED CT: **Arachnodactyly** (62250003); Spider finger (62250003); Dolichostenomelia (62250003); Congenital **arachnodactyly** (62250003)

HPO: HP:0001166

Image

details

Definition Go to:

A tall and slim body build with increased arm span to height ratio (>1.05) and a reduced upper-to-lower segment ratio (<0.85), i.e., unusually long arms and legs. The extremities as well as the hands and feet are unusually slim. [from HPO]

Table of contents

- Definition
- Term Hierarchy
- Conditions with this feature
- Recent clinical studies
- Recent systematic reviews

Genetic Testing Registry

- Deletion/duplication analysis (10)
- Sequence analysis of the entire coding region (10)
- See all (10)

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Conditions with the clinical feature: Arachnodactyly

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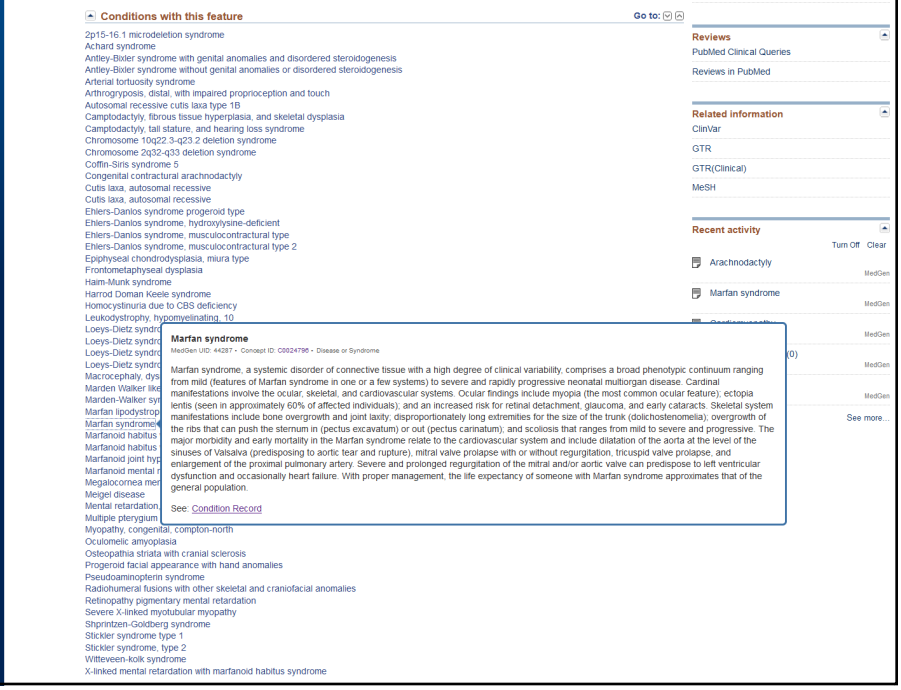

Advanced search: add multiple parameters

- Clinical features
- Genes
- Chromosomal locations
- Mode of inheritance
- OMIM#

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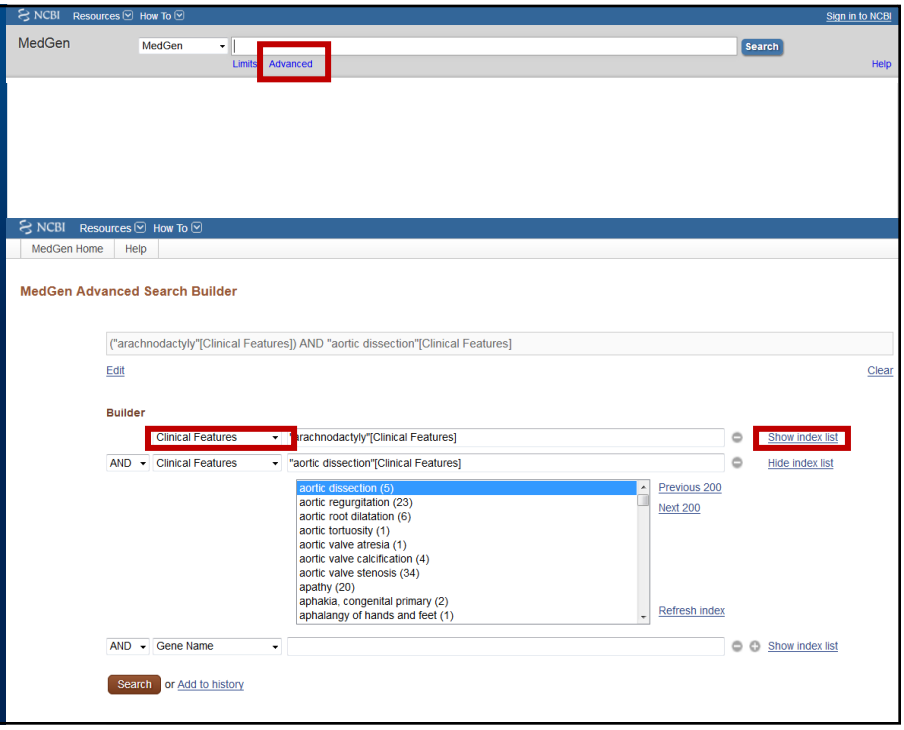
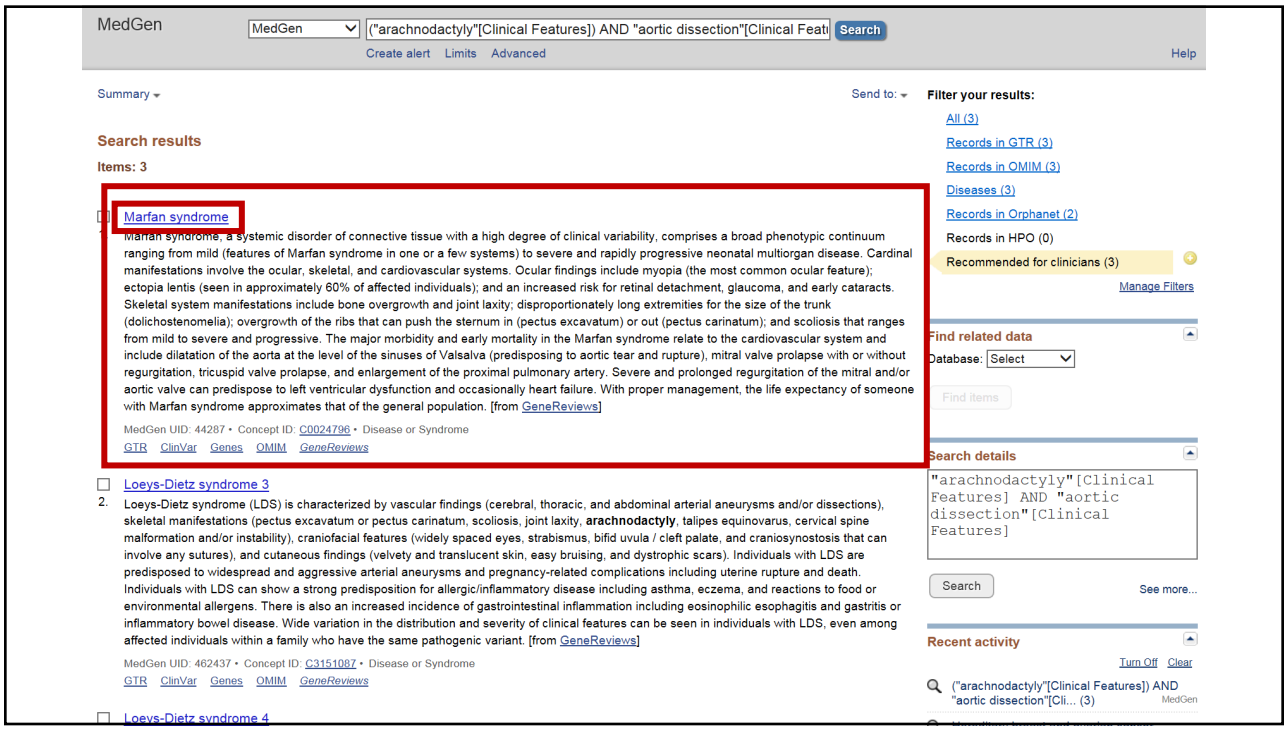
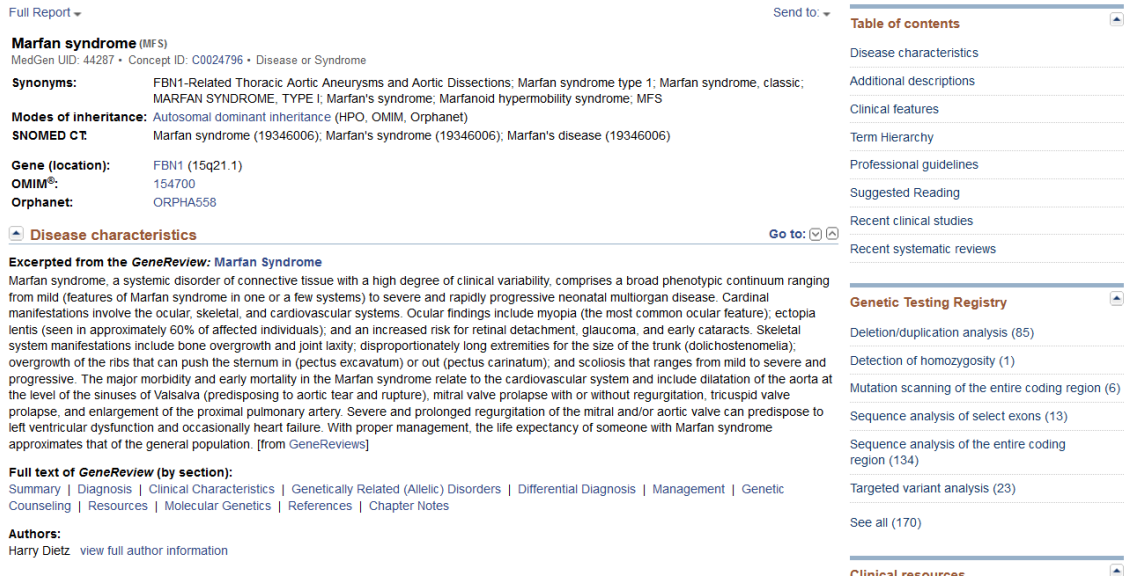




MedGen Disease Record



Full Report ▾ Send to: ▾

Marfan syndrome (MFS)
MedGen UID: 44287 • Concept ID: C0024796 • Disease or Syndrome

Synonyms: FBN1-Related Thoracic Aortic Aneurysms and Aortic Dissections; Marfan syndrome type 1; Marfan syndrome, classic; MARFAN SYNDROME, TYPE I; Marfan's syndrome; Marfanoid hypermobility syndrome; MFS
Modes of inheritance: Autosomal dominant inheritance (HPO, OMIM, Orphanet)
SNOMED CT: Marfan syndrome (19346006); Marfan's syndrome (19346006); Marfan's disease (19346006)

Gene (location): FBN1 (15q21.1)
OMIM®: 154700
Orphanet: ORPHA558

Disease characteristics Go to:

Excerpted from the *GeneReview:* Marfan Syndrome
Marfan syndrome, a systemic disorder of connective tissue with a high degree of clinical variability, comprises a broad phenotypic continuum ranging from mild (features of Marfan syndrome in one or a few systems) to severe and rapidly progressive neonatal multiorgan disease. Cardinal manifestations involve the ocular, skeletal, and cardiovascular systems. Ocular findings include myopia (the most common ocular feature); ectopia lentis (seen in approximately 60% of affected individuals); and an increased risk for retinal detachment, glaucoma, and early cataracts. Skeletal system manifestations include bone overgrowth and joint laxity; disproportionately long extremities for the size of the trunk (dolichostenomelia); overgrowth of the ribs that can push the sternum in (pectus excavatum) or out (pectus carinatum); and scoliosis that ranges from mild to severe and progressive. The major morbidity and early mortality in the Marfan syndrome relate to the cardiovascular system and include dilatation of the aorta at the level of the sinuses of Valsalva (predisposing to aortic tear and rupture), mitral valve prolapse with or without regurgitation, tricuspid valve prolapse, and enlargement of the proximal pulmonary artery. Severe and prolonged regurgitation of the mitral and/or aortic valve can predispose to left ventricular dysfunction and occasionally heart failure. With proper management, the life expectancy of someone with Marfan syndrome approximates that of the general population. [from GeneReviews]

Full text of *GeneReview* (by section):
Summary | Diagnosis | Clinical Characteristics | Genetically Related (Allelic) Disorders | Differential Diagnosis | Management | Genetic Counseling | Resources | Molecular Genetics | References | Chapter Notes

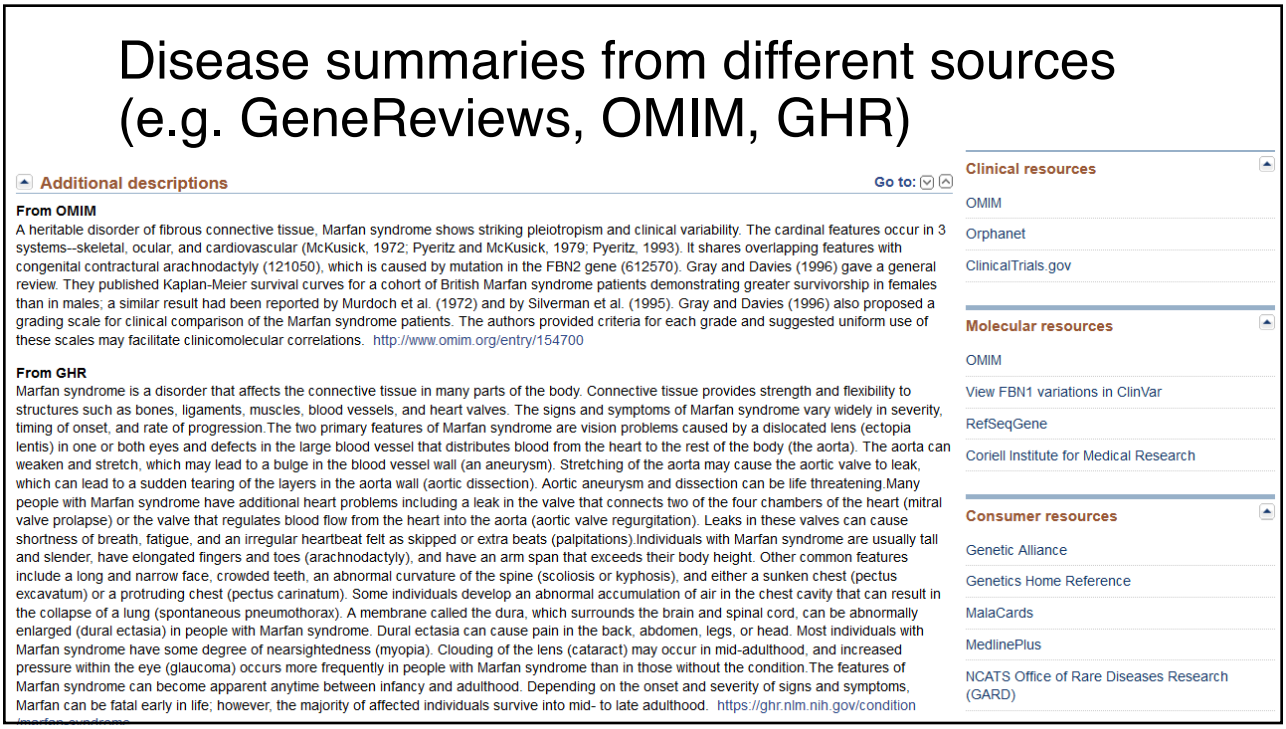
Authors:
Harry Dietz view full author information

Table of contents
Disease characteristics
Additional descriptions
Clinical features
Term Hierarchy
Professional guidelines
Suggested Reading
Recent clinical studies
Recent systematic reviews

Genetic Testing Registry
Deletion/duplication analysis (85)
Detection of homozygosity (1)
Mutation scanning of the entire coding region (6)
Sequence analysis of select exons (13)
Sequence analysis of the entire coding region (134)
Targeted variant analysis (23)
See all (170)

Clinical resources

Disease summaries from different sources (e.g. GeneReviews, OMIM, GHR)



Additional descriptions Go to:

From OMIM
A heritable disorder of fibrous connective tissue, Marfan syndrome shows striking pleiotropism and clinical variability. The cardinal features occur in 3 systems--skeletal, ocular, and cardiovascular (McKusick, 1972; Pyeritz and McKusick, 1979; Pyeritz, 1993). It shares overlapping features with congenital contractural arachnodactyly (121050), which is caused by mutation in the FBN2 gene (612570). Gray and Davies (1996) gave a general review. They published Kaplan-Meier survival curves for a cohort of British Marfan syndrome patients demonstrating greater survivorship in females than in males; a similar result had been reported by Murdoch et al. (1972) and by Silverman et al. (1995). Gray and Davies (1996) also proposed a grading scale for clinical comparison of the Marfan syndrome patients. The authors provided criteria for each grade and suggested uniform use of these scales may facilitate clinicomolecular correlations. http://www.omim.org/entry/154700

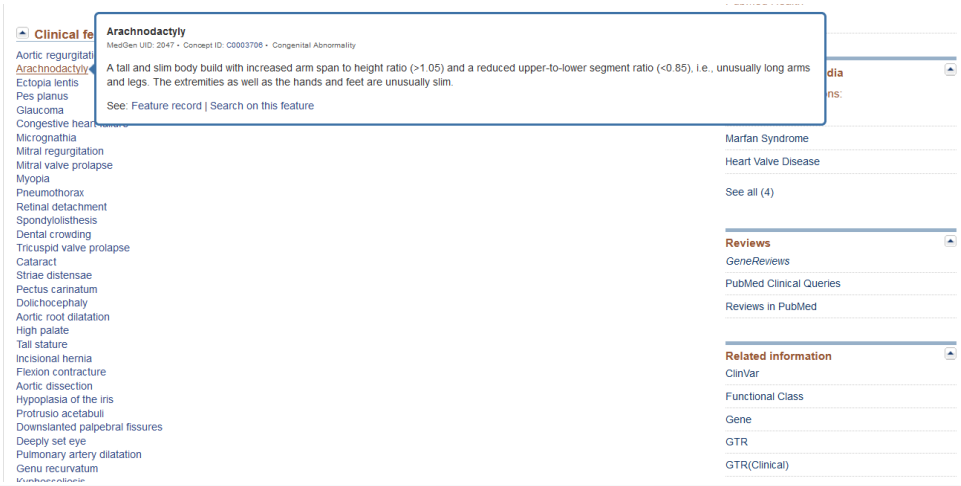
From GHR
Marfan syndrome is a disorder that affects the connective tissue in many parts of the body. Connective tissue provides strength and flexibility to structures such as bones, ligaments, muscles, blood vessels, and heart valves. The signs and symptoms of Marfan syndrome vary widely in severity, timing of onset, and rate of progression.The two primary features of Marfan syndrome are vision problems caused by a dislocated lens (ectopia lentis) in one or both eyes and defects in the large blood vessel that distributes blood from the heart to the rest of the body (the aorta). The aorta can weaken and stretch, which may lead to a bulge in the blood vessel wall (an aneurysm). Stretching of the aorta may cause the aortic valve to leak, which can lead to a sudden tearing of the layers in the aorta wall (aortic dissection). Aortic aneurysm and dissection can be life threatening.Many people with Marfan syndrome have additional heart problems including a leak in the valve that connects two of the four chambers of the heart (mitral valve prolapse) or the valve that regulates blood flow from the heart into the aorta (aortic valve regurgitation). Leaks in these valves can cause shortness of breath, fatigue, and an irregular heartbeat felt as skipped or extra beats (palpitations).Individuals with Marfan syndrome are usually tall and slender, have elongated fingers and toes (arachnodactyly), and have an arm span that exceeds their body height. Other common features include a long and narrow face, crowded teeth, an abnormal curvature of the spine (scoliosis or kyphosis), and either a sunken chest (pectus excavatum) or a protruding chest (pectus carinatum). Some individuals develop an abnormal accumulation of air in the chest cavity that can result in the collapse of a lung (spontaneous pneumothorax). A membrane called the dura, which surrounds the brain and spinal cord, can be abnormally enlarged (dural ectasia) in people with Marfan syndrome. Dural ectasia can cause pain in the back, abdomen, legs, or head. Most individuals with Marfan syndrome have some degree of nearsightedness (myopia). Clouding of the lens (cataract) may occur in mid-adulthood, and increased pressure within the eye (glaucoma) occurs more frequently in people with Marfan syndrome than in those without the condition.The features of Marfan syndrome can become apparent anytime between infancy and adulthood. Depending on the onset and severity of signs and symptoms, Marfan can be fatal early in life; however, the majority of affected individuals survive into mid- to late adulthood. https://ghr.nlm.nih.gov/condition/marfan-syndrome

Clinical resources
OMIM
Orphanet
ClinicalTrials.gov

Molecular resources
OMIM
View FBN1 variations in ClinVar
RefSeqGene
Coriell Institute for Medical Research

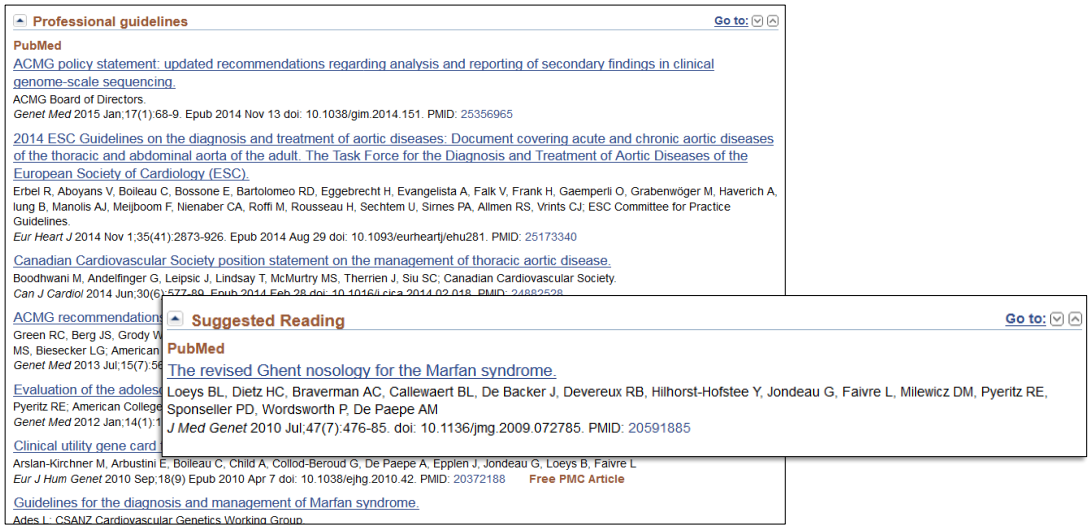
Consumer resources
Genetic Alliance
Genetics Home Reference
MalaCards
MedlinePlus
NCATS Office of Rare Diseases Research (GARD)

List of clinical features for the disease with descriptions (HPO, OMIM)



Disease hierarchy (manually curated, MeSH, Orphanet)

Professional guidelines and suggested articles



Professional guidelines Go to:

PubMed

ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing.
ACMG Board of Directors.
Genet Med 2015 Jan;17(1):68-9. Epub 2014 Nov 13 doi: 10.1038/gim.2014.151. PMID: 25356965

2014 ESC Guidelines on the diagnosis and treatment of aortic diseases: Document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The Task Force for the Diagnosis and Treatment of Aortic Diseases of the European Society of Cardiology (ESC).
Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, Evangelista A, Falk V, Frank H, Gaemperli O, Grabenwöger M, Haverich A, Iung B, Manolis AJ, Meijboom F, Nienaber CA, Roffi M, Rousseau H, Sechtem U, Sirnes PA, Allmen RS, Vrints CJ; ESC Committee for Practice Guidelines.
Eur Heart J 2014 Nov 1;35(41):2873-926. Epub 2014 Aug 29 doi: 10.1093/eurheartj/ehu281. PMID: 25173340

Canadian Cardiovascular Society position statement on the management of thoracic aortic disease.
Boodhwani M, Andelfinger G, Leipsic J, Lindsay T, McMurtry MS, Therrien J, Siu SC; Canadian Cardiovascular Society.
Can J Cardiol 2014 Jun;30(6):577-89. Epub 2014 Feb 28 doi: 10.1016/j.cjca.2014.02.018. PMID: 24882528

ACMG recommendations
Green RC, Berg JS, Grody W
MS, Biesecker LG; American
Genet Med 2013 Jul;15(7):56

Evaluation of the adoles
Pyeritz RE; American College
Genet Med 2012 Jan;14(1):1

Clinical utility gene card
Arslan-Kirchner M, Arbustini E, Boileau C, Child A, Collod-Beroud G, De Paepe A, Epplen J, Jondeau G, Loeys B, Faivre L
Eur J Hum Genet 2010 Sep;18(9) Epub 2010 Apr 7 doi: 10.1038/ejhg.2010.42. PMID: 20372188 **Free PMC Article**

Guidelines for the diagnosis and management of Marfan syndrome.
Ades L; CSANZ Cardiovascular Genetics Working Group

Suggested Reading Go to:

PubMed

The revised Ghent nosology for the Marfan syndrome.
Loeys BL, Dietz HC, Braverman AC, Callewaert BL, De Backer J, Devereux RB, Hilhorst-Hofstee Y, Jondeau G, Faivre L, Milewicz DM, Pyeritz RE, Sponseller PD, Wordsworth P, De Paepe AM
J Med Genet 2010 Jul;47(7):476-85. doi: 10.1136/jmg.2009.072785. PMID: 20591885

PubMed Clinical Queries about diagnosis, etiology, therapy, prognosis, systematic reviews

Recent clinical studies Go to:

Etiology

The effects of acute and elective cardiac surgery on the anxiety traits of patients with Marfan syndrome.
Benke K, Ágg B, Pólos M, Sayour AA, Radovits T, Bartha E, Nagy P, Rákóczi B, Koller Á, Szokolai V, Hedberg J, Merkely B, Nagy ZB, Szabolcs Z
BMC Psychiatry 2017 Jul 17;17(1):253. doi: 10.1186/s12888-017-1417-9. PMID: 28716062 **Free PMC Article**

Relationship between fibrillin-1 genotype and severity of cardiovascular involvement in Marfan syndrome.
Franken R, Teixido-Tura G, Brion M, Forteza A, Rodriguez-Palomares J, Gutierrez L, Garcia Dorado D, Pals G, Mulder BJ, Evangelista A
Heart 2017 Nov;103(22):1795-1799. Epub 2017 May 3 doi: 10.1136/heartjnl-2016-310631. PMID: 28468757

Pregnancy-related acute aortic dissection in Marfan syndrome: A review of the literature.
Smith K, Gros B
Congenit Heart Dis 2017 May;12(3):251-260. Epub 2017 Apr 2 doi: 10.1111/chd.12465. PMID: 28371362

Aortic events in a nationwide Marfan syndrome cohort.
Groth KA, Stochholm K, Hove H, Kyhl K, Gregersen PA, Vejlstrup N, Østergaard JR, Gravholt CH, Andersen NH
Clin Res Cardiol 2017 Feb;106(2):105-112. Epub 2016 Aug 22 doi: 10.1007/s00392-016-1028-3. PMID: 27550511

Long-term outcomes of aortic root operations for Marfan syndrome: A comparison of Bentall versus aortic valve-sparing procedures.
Price J, Magruder JT, Young A, Grimm JC, Patel ND, Alejo D, Dietz HC, Vricella LA, Cameron DE
J Thorac Cardiovasc Surg 2016 Feb;151(2):330-6. Epub 2015 Oct 27 doi: 10.1016/j.jtcvs.2015.10.068. PMID: 26704057

See all (1440)

Diagnosis

The effects of acute and elective cardiac surgery on the anxiety traits of patients with Marfan syndrome.
Benke K, Ágg B, Pólos M, Sayour AA, Radovits T, Bartha E, Nagy P, Rákóczi B, Koller Á, Szokolai V, Hedberg J, Merkely B, Nagy ZB, Szabolcs Z
BMC Psychiatry 2017 Jul 17;17(1):253. doi: 10.1186/s12888-017-1417-9. PMID: 28716062 **Free PMC Article**

A Novel Fibrillin-1 Gene Mutation Leading to Marfan Syndrome in a Korean Girl.
Nam HK, Nam MH, Ha KS, Rhie YJ, Lee KH
Ann Clin Lab Sci 2017 Mar;47(2):221-225. PMID: 28442527

Relevant links at your fingertips

U.S. National Library of Medicine
National Center for Biotechnology Information

Genetic Testing Registry

- Deletion/duplication analysis (85)
- Detection of homozygosity (1)
- Mutation scanning of the entire coding region (6)
- Sequence analysis of select exons (13)
- Sequence analysis of the entire coding region (134)
- Targeted variant analysis (23)

See all (170)

Clinical resources

- OMIM
- Orphanet
- ClinicalTrials.gov

Molecular resources

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- View FBN1 variations in ClinVar
- RefSeqGene
- Coriell Institute for Medical Research

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Relevant links at your fingertips

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National Center for Biotechnology Information

Consumer resources

- Genetic Alliance
- Genetics Home Reference
- MalaCards
- MedlinePlus
- NCATS Office of Rare Diseases Research (GARD)
- PubMed Health
- Marfan Syndrome

Medical Encyclopedia

Diseases & Conditions:

- Mitral Valve Prolapse
- Marfan Syndrome
- Heart Valve Disease

See all (4)

Reviews

- *GeneReviews*
- PubMed Clinical Queries
- Reviews in PubMed

Related information

- ClinVar
- Functional Class
- Gene
- GTR
- GTR(Clinical)
- MeSH
- NCBI Bookshelf
- OMIM
- OMIM(Genes)
- Pathways + GO
- PubMed (Bookshelf cited)
- PubMed (GeneReviews)
- PubMed (OMIM)

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MedGen as terminology service

Aggregates and harmonizes genetic phenotype information

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- Phenotype backbone of
  - NIH Genetic Testing Registry (GTR, https://www.ncbi.nlm.nih.gov/gtr) test descriptions
  - ClinVar (https://www.ncbi.nlm.nih.gov/clinvar) variant interpretations
- Computational access through ftp reports (ftp://ftp.ncbi.nlm.nih.gov/pub/medgen/) and NCBI's API, e-utilities (esearch and esummary)
- Hospital/clinic systems can use NCBI's API to tailor views of genetic information for their users at point of care

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How can MedGen help the clinical process?

- Prepare for a clinic visit
  - Research a phenotype: one page has all freely available information about a condition, phenotype or drug response from authoritative sources
  - Help suggest conditions that fit the cluster of clinical features for a patient
- During a clinic visit
  - List clinical features to evaluate a patient for a suspected diagnosis
  - Actionable links to professional practice guidelines, clinicaltrials.gov
  - Links to available tests for the condition
  - Therapeutic recommendations for drug responses based on genotype from professional societies
- After a clinic visit
  - Links to ClinVar for help with variant interpretation
- Links to consumer resources to educate the patient and family about the diagnosis

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- URLs & Places to Learn More -

MedGen: https://www.ncbi.nlm.nih.gov/medgen

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NCBI Insights Blog: ncbiinsights.ncbi.nlm.nih.gov

YouTube
User: NCBINLM

For help with MedGen:
medgen_help@ncbi.nlm.nih.gov

Questions?